

# CPAP in the Perioperative Setting

## Evidence of Support



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OSA is a commonly encountered comorbid condition in surgical patients. The risk of cardio-pulmonary complications is increased by two to threefold with OSA. Among the different treatment options for OSA, CPAP is an efficacious modality. This review examines the evidence regarding the use of CPAP in the preoperative and postoperative periods in surgical patients with diagnosed and undiagnosed OSA.

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**KEY WORDS:** CPAP; OSA; perioperative period

OSA is a prevalent sleep breathing disorder in the general population with estimated prevalence of at least 9% to 25%.<sup>1</sup> Indeed, in a recent population-based study in Switzerland, the prevalence of moderate to severe OSA was 23.4% in women and 49.7% in men.<sup>2</sup> The prevalence of OSA in surgical patients using International Classification of Disease-9 codes has been reported to be 7% to 10%.<sup>3-5</sup> However, using polysomnography (PSG), the prevalence of OSA in surgical patients is expected to be significantly higher than simply using International Classification of Disease-9 codes from administrative databases. Indeed, the prevalence may be as high as 70% in high-risk populations such as patients undergoing bariatric surgery.<sup>6,7</sup> Surgical patients with OSA pose a significant clinical challenge to health-care professionals

because of OSA's associations with several comorbidities, including cardiovascular disease, heart failure, arrhythmias, hypertension, stroke, and metabolic syndrome.<sup>8-11</sup> During the perioperative period, sleep is disrupted and the severity of sleep-disordered breathing (SDB) is increased postoperatively in surgical patients with OSA.<sup>12,13</sup>

The American Society of Anesthesiologists published a practice guideline recommending preoperative screening to identify undiagnosed OSA, preoperative initiation of CPAP if possible, and postoperative monitoring of patients with OSA.<sup>14,15</sup> Perioperative complications related to OSA are increasingly linked to malpractice lawsuits with severe financial penalties.<sup>16,17</sup> The lack of evidence behind the guideline recommendations and

**ABBREVIATIONS:** AHI = apnea hypopnea index; APAP = autotitrated positive airway pressure; PACU = postanesthesia care unit; RCTs = randomized controlled trials; RR = risk reduction; SDB = sleep-disordered breathing

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the significant cost of guideline implementation have created a dilemma between potentially improved postoperative adverse events and increased health-care resource utilization. In practice, fewer than 20% of patients with a diagnosis of OSA receive CPAP therapy, are observed in advanced care settings, or both.<sup>18</sup> This review examines the evidence regarding the use of CPAP in the preoperative and postoperative periods in surgical patients with diagnosed and undiagnosed OSA.

## Surgical Patients With OSA and Perioperative Complications

A close relationship exists among OSA, sleep, and anesthesia. Upper airway behavior during sleep serves to some extent as a surrogate of airway behavior during anesthesia and recovery from anesthesia. Likewise, upper airway abnormalities observed by anesthesiologists during the perioperative period is likely to predict upper airway behavior during sleep.<sup>19</sup> A patient with an upper airway that is prone to collapse may also be at increased risk of compromised arousal mechanism in the postoperative period. Several large database studies and two meta-analysis have shown that patients with OSA have increased risk of postoperative complications.<sup>3,4,20-25</sup> Two recent meta-analysis of 13 and 17 studies indicate that, compared with patients with OSA, patients with OSA have a higher incidence of respiratory complications, postoperative cardiac events, and increased ICU transfer.<sup>24,25</sup> In line with the meta-analysis, five recent studies using data from large national and international databases including millions of patients demonstrated a significantly increased risk of atrial fibrillation, respiratory failure, aspiration pneumonia, ARDS, increased emergent postoperative endotracheal intubation, and need for postoperative ventilation among patients with a diagnosis of OSA vs control subjects.<sup>3,4,20-22,26</sup> D'Apuzzo et al<sup>20</sup> demonstrated that there is increased mortality in OSA vs patients without OSA undergoing revision joint arthroplasty (OR, 1.9;  $P = .002$ ). That this study included patients undergoing revision arthroplasty may suggest a higher burden of comorbidities. Paradoxically, the increased risk of cardiopulmonary complications did not translate into increased risk of in-hospital mortality in two studies.<sup>4,20</sup> There may be several reasons behind the reduction in in-hospital mortality: (1) patients with OSA may have received more vigilant care; (2) patients

with OSA may have exhibited signs of deterioration earlier in their hospital course; (3) the reason behind respiratory failure in patients with OSA may have been easier to treat (eg, respiratory failure from upper airway compromise vs aspiration pneumonia or ARDS); or (4) in the control group, patients may have undiagnosed OSA with increased risk of mortality and morbidity. Indeed, in two studies of postsurgical patients,<sup>4,20</sup> those with an OSA diagnosis who developed respiratory failure were intubated earlier and received mechanical ventilation for a shorter period, suggesting that the cause of respiratory failure was rapidly reversible, perhaps related to upper airway complications resulting from sedatives and opioid analgesics.

In the general population, a significant proportion of patients with moderate to severe OSA remains undiagnosed.<sup>27</sup> This corollary may also apply to the surgical patients in the perioperative period. In a retrospective nested cohort study, preoperative screening followed by PSG was performed to identify patients with OSA, and the results were blinded to the perioperative care team. Both anesthesiologists and surgeons failed to identify a majority of the newly diagnosed patients with moderate to severe OSA.<sup>28</sup> Patients with undiagnosed OSA presenting for surgery may have further increase in cardiopulmonary complications.<sup>29-31</sup>

## Postoperative Use of CPAP in Surgical Patients Without OSA

The efficacy of CPAP in patients without a diagnosis of OSA has been well-established by a recent meta-analysis of nine randomized controlled trials (RCTs) in patients undergoing abdominal surgery.<sup>32</sup> These studies have shown that perioperative use of CPAP leads to a reduction in the rate of postoperative pulmonary complications. In 200 patients who developed hypoxemia immediately after undergoing major abdominal surgery, the use of postoperative CPAP at 7.5 cm H<sub>2</sub>O plus supplemental oxygen using a helmet interface led to a reduction in the incidence of endotracheal intubation, pneumonia, infection, and sepsis when compared with supplemental oxygen alone.<sup>33</sup> Significant reduction in the rate of pulmonary complications with the prophylactic use of nasal CPAP was also demonstrated in patients undergoing thoracoabdominal aortic surgery and cardiac surgery.<sup>34,35</sup>

## Preoperative and Postoperative CPAP in Surgical Patients With OSA

The number of surgical cases performed globally is increasing, and an estimated 250 million major surgeries are being performed each year.<sup>36</sup> With the global rise of obesity, the prevalence of OSA will likely continue to rise.<sup>1,2</sup> Perioperative care of patients with OSA will be an increasing challenge. The concept of perioperative surgical home, encompassing optimization of surgical patient's health status from preoperative period to postoperative discharge care for conditions, such as coronary heart disease, congestive heart failure, COPD, or diabetes, has become the new reality.<sup>37</sup> The same concept applies to patients with suspected or diagnosed OSA presenting for surgery, where the association of OSA with postoperative complications has been a wake-up call for action.<sup>38</sup> Anesthesiologists are in an ideal position to identify patients with SDB, optimize their perioperative management, and contribute to their continuum of care. Because CPAP therapy has long-term health benefits for patients with OSA, preoperative clinics may provide an opportunity for identification of patients with undiagnosed OSA and initiation of treatment. In a recent study, surgical patients were screened for OSA in a preoperative clinic and were offered CPAP therapy. Those who were CPAP-adherent had better sleep quality, less daytime sleepiness, and reduction of medication usage for associated medical diseases.<sup>39</sup> For patients with OSA presenting for surgery, perioperative clinicians may face a variety of scenarios: patients with (1) diagnosed OSA with appropriate adherence to effective therapy, (2) diagnosed OSA but not adherent to prescribed therapy, and (3) undiagnosed OSA. Patients who are treated and adherent to CPAP should continue their CPAP in the postoperative period. Those patients with diagnosed OSA who are not adherent to therapy or undiagnosed OSA pose a more significant clinical challenge.

### *Effects of CPAP on Postoperative Outcomes in Surgical Patients With OSA*

In patients with OSA, CPAP has been shown to have beneficial effects on postoperative adverse events. In a case series by Rennotte et al<sup>40</sup>, two patients with OSA without CPAP suffered postoperative adverse events and one patient died, whereas 14 patients with OSA treated with CPAP had uneventful postoperative courses. In a retrospective case-control study, patients with OSA without CPAP had more postoperative complications than patients with OSA treated with CPAP (44% vs 27%,  $P = .02$ ). Unplanned ICU transfer was also significantly

higher in patients with OSA without CPAP treatment and length of stay was 1 day longer.<sup>41</sup> In a retrospective cohort match study, Liao et al<sup>42</sup> found that 30% of the patients with OSA not using home CPAP developed an adverse event such as upper airway obstruction or hypoxemia, resulting in the initiation of postoperative CPAP. Studies on the efficacy of CPAP on postoperative outcomes are shown in Table 1.<sup>30,31,40-46</sup>

A recent meta-analysis of six studies including 904 patients examined the effectiveness of CPAP therapy on postoperative outcomes, postoperative apnea hypopnea index (AHI), and length of stay in surgical patients with OSA plus CPAP therapy vs patients with OSA without CPAP therapy.<sup>47</sup> There was no significant difference in postoperative adverse events between the CPAP and no-CPAP groups (risk ratio, 0.88; 95% CI, 0.73-1.06;  $P = .19$ ). Patients with OSA who used CPAP either preoperatively and/or postoperatively compared with no-CPAP had a risk ratio of 0.88 (0.73-1.06) and a 12% risk reduction of postoperative adverse events with a corresponding number needed to treat to benefit of 45.<sup>47</sup> The nonsignificant benefit of CPAP on postoperative adverse events may have been related to the relatively small sample size of 904 patients and an overall low incidence of postoperative complications in the meta-analysis. Other potential reasons may have been suboptimal CPAP adherence in the perioperative period. However, the meta-analysis revealed that perioperative CPAP significantly reduced postoperative AHI from the preoperative baseline AHI (preoperative AHI vs postoperative AHI:  $37 \pm 19$  vs  $12 \pm 16$  events/h).<sup>47</sup> There was also a trend toward significance for reduction in the length of hospital stay of 0.4 days favoring the CPAP group (CPAP vs no-CPAP:  $4.0 \pm 4$  vs  $4.4 \pm 8$  days,  $P = .05$ ).<sup>47</sup>

Even though five studies supported the use of CPAP in the perioperative period, they were not included in the meta-analysis by Nagappa et al<sup>47</sup> (Table 2), because of a lack of data in either the study group and/or control group. In a retrospective chart review by Meng et al,<sup>48</sup> patients who did not use CPAP had a significantly higher incidence of postoperative hypertension (CPAP vs no-CPAP group: 18% vs 29%;  $P = .013$ ) and oxygen desaturations (CPAP vs no-CPAP group: 5% vs 43%;  $P = .012$ ). Also, the length of postanesthesia care unit (PACU) stay was longer in the no-CPAP group when compared with the CPAP group ( $211 \pm 82$  min vs  $159 \pm 78$  min,  $P = .029$ ). Neligan et al<sup>49</sup> conducted an RCT on morbidly obese patients with OSA undergoing laparoscopic bariatric surgery. The administration of

**TABLE 1 ] Effect of CPAP on Postoperative Outcomes in Surgical Patients With OSA**

Author	Study Type	No.	Result
Rennotte et al, 1995 <sup>40</sup>	Case series report	16	No-CPAP vs CPAP: 2 vs 14 First patient died; second patient: serious postop Cx 14 patients nasal CPAP Rx, no Cx
Gupta et al, 2001 <sup>41</sup>	Retrospective case-control study	101	No-CPAP vs CPAP group: 68 vs 33 Any Cx: 44% vs 27% ( $P = .1$ ) Serious Cx: 31% vs 9% ( $P = .02$ ) Total ICU stay: 32.3% vs 3% ( $P = .001$ ) Unplanned ICU stay: 27.9% vs 3% ( $P = .003$ ) Hospital stay: $7 \pm 3$ vs $6 \pm 2$ days ( $P = .03$ )
Jensen et al, 2008 <sup>43</sup>	Prospective cohort study	284	No-CPAP/BiPAP vs CPAP/BiPAP: 140 vs 144 Pneumonia: 2.1% vs 0.7% (NS) Hospital stay: 2.2 vs 2.7 days ( $P = .244$ )
Liao et al, 2009 <sup>42</sup>	Retrospective matched-cohort study	480	OSA vs non-OSA: 240 vs 240 Postop Cx: 44% vs 28% ( $P < .05$ ) $SpO_2 < 90\%$ : 17% vs 8% No-CPAP vs CPAP: 90 vs 150 Postop Cx: 46.6% vs 40.6% ( $P = .36$ )
Liao et al, 2013 <sup>44</sup>	RCT	177	No-APAP vs APAP: 90 vs 87 Postoperative Cx: 48.3% vs 48.3% ( $P = .939$ ) Preoperative AHI vs postoperative AHI (NS) APAP: 30.1 to 3.0 ( $P < .001$ ) No-APAP: 30.4 to 31.9 ( $P = .302$ ) Hospital stay: $4.3 \pm 5.5$ vs $3.5 \pm 6.2$ days ( $P = .36$ )
O'Gorman et al, 2013 <sup>45</sup>	RCT	138	No-APAP vs APAP Any Cx: 20.9% vs 23.3% ( $P = 1.0$ ) No significant difference between LOS ( $P = .65$ )
Mutter et al, 2014 <sup>30</sup>	Matched-cohort study	20,488	Respiratory Cx Overall: 2.08, 95% CI, 1.35-2.19, $P = .0008$ Diagnosed OSA vs undiagnosed OSA OR, 0.68; 95% CI, 0.27-1.71; $P = .41$ Cardiovascular Cx Undiagnosed OSA vs matched cohort control OR, 2.20; 95% CI, 1.16-4.17; $P = .02$ Diagnosed OSA vs matched cohort control OR, 0.75; 95% CI, 0.43-1.28; $P = .29$ Diagnosed OSA vs undiagnosed OSA OR, 0.34; 95% CI, 0.15-0.77; $P = .009$
Abdelsattar et al, 2015 <sup>31</sup>	Prospective cohort study	2646	Untreated OSA vs treated OSA: 1,465 vs 1,181 Cardiopulmonary Cx 6.7% vs 4.0%; aOR, 1.8; $P = .001$ Unplanned reintubations aOR, 2.5; $P = .003$ Myocardial infarction aOR, 2.6; $P = .031$
Proczko et al, 2014 <sup>46</sup>	Retrospective cohort	693	Diagnosed OSA and Rx with CPAP vs STOP-Bang $\geq 3$ 99 vs 182 Hypertension 11.1% vs 11.5% ( $P = .9142$ ) Death: 0% vs 1% ( $P = .5142$ ) Hospital stay: 3.2 vs 4.1 days ( $P < .0001$ ) Pneumonia: 2% vs 9.3% ( $P < .04$ ) Reintubation: 0% vs 3.8% ( $P = .1442$ ) ICU admission: 0% vs 1% ( $P = .5142$ )

AHI = apnea hypopnea index; aOR = adjusted odds ratio; APAP = autotitrated positive airway pressure; BiPAP = bilevel positive airway pressure; Cx = complications; LOS = length of hospital stay; NS = not significant; RCT = randomized controlled trial; Rx = treated;  $SpO_2$  = oxygen saturation; STOP-Bang = snoring, tired, observed, pressure, BMI, age > 50 years, neck size large, gender.

**TABLE 2 ] Additional Studies That Supported the Use of CPAP in Surgical Patients With OSA**

Author	Study Type and Surgical Procedure	No.	Result
Ramirez et al, 2009 <sup>52</sup>	Retrospective review Roux-en-Y gastric bypass	310	Postoperative CPAP vs no-CPAP: 91 vs 219 Basal atelectasis: 3.3% vs 1.8% ( $P > .05$ ) Wound infection: 4.4% vs 0.45% ( $P > .05$ ) GI bleeding: 0% vs 0.45% (NS) Overall morbidity: 4.5% vs 3.6% ( $P > .05$ )
Hallowell et al, 2007 <sup>50</sup>	Retrospective review Bariatric surgery	890	Selective OSA testing (1998-2003) vs mandatory OSA testing and perioperative CPAP Rx (2004-2005) Respiratory-related ICU stay 34% vs 9% ( $P < .001$ )
Meng et al, 2010 <sup>48</sup>	Retrospective review Roux-en-Y gastric bypass	356	Perioperative CPAP (102) vs no-CPAP (254) Nausea in PACU: 36% vs 35% ( $P = .91$ ) Emesis in PACU: 19% vs 17% ( $P = .8$ ) Hypertension: 18% vs 29% ( $P = .013$ ) O <sub>2</sub> disturbance: 5% vs 13% ( $P = .012$ ) PACU stay: 159 ± 78 vs 211 ± 82 ( $P = .029$ ) Reintubation: 2% vs 5% ( $P = .45$ ) ICU admission: 2% vs 5% ( $P = .45$ )
Neligan et al, 2009 <sup>49</sup>	RCT	40	Postextubation CPAP vs PACU CPAP FEV <sub>1</sub> : coefficient, 0.37; SE, 0.13; $P < .003$ ; 95% CI, 0.13-0.62 FVC: coefficient, 0.39; SE, 0.14; $P < .006$ ; 95% CI, 0.11-0.66 PEFR: coefficient, 0.82; SE, 0.31; $P < .008$ ; 95% CI, 0.21-0.1.4
Huerta et al, 2002 <sup>51</sup>	Prospective review Roux-en-Y gastric bypass	1067	No correlation between CPAP use and anastomotic leak ( $P = .06$ )

PACU = postanesthesia care unit; PEFR = peak expiratory flow rate. See Table 1 legend for expansion of other abbreviations.

CPAP immediately after extubation improved spirometric lung functions at 1 h and 24 h after extubation in the operating room vs CPAP that was started in the PACU. Hallowell et al<sup>50</sup> found that compulsory screening for OSA and perioperative treatment with CPAP therapy decreased respiratory-related ICU stays from 34% to 1% ( $P < .001$ ). Huerta et al<sup>51</sup> prospectively evaluated 420 patients with OSA undergoing bariatric surgery, of which 159 patients were dependent on CPAP. There were no respiratory complications and no positive correlations between CPAP use and anastomotic leak. This suggests that CPAP is an effective tool for treating hypoventilation after gastric bypass without necessarily increasing the risk of postoperative anastomotic leaks.<sup>51</sup> However, after laparoscopic Roux-en-Y gastric bypass, Ramirez et al<sup>52</sup> found that there was no significant difference in the overall morbidity between those who used CPAP postoperatively and those who did not (4.5% vs 3.5%,  $P > .05$ ).

Two recent large studies further support the benefits of CPAP in patients with diagnosed and undiagnosed OSA.<sup>30,31</sup> Mutter et al<sup>30</sup> linked a clinical database of PSG data for patients with newly diagnosed OSA with a CPAP prescription to a large provincial health

administrative database and compared postoperative outcomes in patients with OSA, before and after OSA diagnosis, with matched control subjects from the general population who had a low risk of having OSA. Patients diagnosed with OSA had significantly reduced risk of cardiovascular adverse events vs undiagnosed patients with OSA (OR, 0.34, 95% CI, 0.15-0.77,  $P = .009$ ). The risk of cardiovascular complications, primarily cardiac arrest and shock, was significantly different between 1,489 undiagnosed OSA (OR, 2.20; 95% CI, 1.16-4.17;  $P = .02$ ) and 2,496 patients diagnosed with OSA (OR, 0.75; 95% CI, 0.43-1.28;  $P = .29$ ). Patients with a preoperative diagnosis of OSA and preoperative prescription for CPAP were less than half as likely to experience cardiovascular complications as those diagnosed after surgery.<sup>30</sup> The risk of respiratory complications (OR, 2.08; 95% CI, 1.35-3.19;  $P < .001$ ) was increased in both 2,629 patients with diagnosed OSA and 1,569 patients with undiagnosed OSA. Most importantly, only patients with severe or undiagnosed OSA had a significantly increased risk of respiratory and cardiovascular complications. This is the first study to show a positive association between the severity of OSA and postoperative risks. Prior negative studies were



likely because of inadequate statistical power.<sup>53-55</sup> Given the association between the severity of OSA and postoperative outcomes, efforts targeting patients with moderate-to-severe undiagnosed OSA in preoperative screening may be more clinically relevant.<sup>56-61</sup>

In another supporting study, Abdelsattar et al<sup>31</sup> prospectively collected data from the Michigan Surgical Quality Collaborative of 52 community and academic hospitals in Michigan to compare postoperative 30-day cardiopulmonary complications between treated and untreated patients with OSA. Adult patients undergoing various general or vascular surgeries were classified into three groups: (1) no diagnosis or a low risk of OSA, (2) documented OSA without therapy or suspicion of OSA (snoring, tired, observed, pressure, BMI, age > 50 years, neck size large, gender [STOP-Bang] score  $\geq 3$  of 8), and (3) diagnosis of OSA with treatment (ie, positive airway pressure [PAP] therapy). Of 26,842 patients, 2,646 (9.9%) had a diagnosis or suspicion of OSA and 55% of them were untreated. Compared with patients with OSA undergoing PAP therapy, documented OSA without therapy or suspicion of OSA was associated with higher cardiopulmonary complications (risk-adjusted rates, 6.7% vs 4%; adjusted OR, 1.8;  $P = .001$ ).<sup>31</sup> Other significant predictors of adverse cardiopulmonary outcomes were older age, higher American Society of Anesthesiologists classes, vascular surgery, and comorbidity index. Both myocardial infarction (adjusted OR, 2.6;  $P = .031$ ) and unplanned reintubations (adjusted OR, 2.5;  $P = .003$ ) were significantly higher in untreated patients with OSA. These two large database studies provide incremental evidence that confirm the benefits of establishing an OSA diagnosis preoperatively and provide a solid rationale for treating OSA with CPAP during the perioperative period.<sup>30,31</sup>

#### *Prospective Clinical Trials of PAP Therapy in Surgical Patients With Undiagnosed OSA or Untreated OSA*

Starting treatment with autotitrating positive airway pressure (APAP) can be as effective as CPAP treatment with PSG titration.<sup>62-64</sup> Because of possible fluid shifts, supine body position, and sedative effects of residual anesthetics and narcotics, a single fixed CPAP pressure setting may not be equally effective in the perioperative environment.<sup>65-68</sup>

Empiric APAP therapy has been studied in three studies<sup>44,45,69</sup> and successfully applied in the

perioperative care of patients at risk for OSA (Table 3). In the study by Guralnick et al<sup>69</sup>, surgical patients with a STOP-Bang score of 3 or higher were referred to undergo split night PSG and received APAP treatment preoperatively. In an RCT, Liao et al<sup>44</sup> investigated the feasibility and effectiveness of perioperative APAP in newly diagnosed untreated patients with OSA. APAP treatment was started 3 days preoperatively, allowing adaptation to the device and continued in the postoperative period for 5 days. O’Gorman et al<sup>45</sup> applied postoperative APAP empirically to orthopedic patients who were considered at high risk of OSA without preoperative PSG or PAP adaptation.

APAP treatment was shown to significantly reduce postoperative AHI and improve oxygen saturation (SpO<sub>2</sub>) in patients with moderate and severe OSA.<sup>44</sup> Although APAP improved obstructive apneas and hypopneas, a full resolution of SDB did not occur in these studies. The preoperative AHI was reduced by an average of 25 events/h postoperatively. Some residual SDB persisted, with a mean AHI  $12 \pm 16$  events/h in the recent meta-analysis.<sup>47</sup> Brar et al<sup>67</sup> found that 18% of surgical patients spent at least 30 min with SpO<sub>2</sub> < 90% the night following surgery despite the use of their prescribed PAP therapy.<sup>67</sup> The severity of baseline OSA, pre-CPAP SpO<sub>2</sub>, net fluid balance, total IV opioid dose, and central apneas may be the contributing factors to hypoxemia.<sup>12,13,60,65,67</sup> As such, it has been suggested that postoperative oximetry monitoring may be indicated in PAP-treated patients with OSA.<sup>67</sup>

In the meta-analysis of perioperative CPAP use, the length of stay was 0.4 days shorter in the CPAP group vs the no-CPAP group.<sup>47</sup> On the contrary, O’Gorman et al<sup>45</sup> showed that there was no benefit for APAP applied postoperatively to patients who were identified as being at high risk of OSA by screening vs patients who receive usual care. The negative results of the study may be due to a type 2 error, with an inadequate sample size and inadequate oxygen supplementation resulting from diluting effects of high flow induced by APAP.<sup>70</sup>

#### *Barriers to Preoperative Diagnosis of OSA and Perioperative CPAP Therapy in Surgical Patients*

There are several barriers to effective diagnosis and treatment of OSA in the perioperative setting. In both clinical and research settings, a significant proportion of

**TABLE 3 ]** Prospective Clinical Trials of Positive Airway Pressure Therapy in Surgical Patients With Undiagnosed OSA or Untreated OSA

Feature	Guralnick et al, 2012 <sup>69</sup> (n = 211)	Liao et al, 2013 <sup>44</sup> (n = 177)	O'Gorman et al, 2013 <sup>45</sup> (n = 138)
Study type	Retrospective observational study	RCT	RCT
Study objective	CPAP adherence during perioperative period	Effect of APAP on AHI and oxygenation	Effect of APAP on hospital stay and postoperative Cx
Timing of APAP	CPAP started preoperatively, followed for adherence postoperatively	3 days preoperatively and 5 days postoperatively	APAP started in PACU and during night and whenever patient sleeps
Study outcome	Median CPAP adherence 2.5 h/night Optimal pressure $9 \pm 2$ cm H <sub>2</sub> O	APAP adherence 45% Preoperative AHI vs postoperative AHI (NS) APAP: 30.1 to 3.0 ( $P < .001$ ) No-APAP: 30.4 to 31.9 ( $P = .302$ )	Any complications: 20.9 vs 23.3% ( $P = 1.0$ ) LOS median, 5 vs 4 days; $P = .02$
Duration of APAP during first night after surgery	NA	$4.1 \pm 5.3$ h	6.2 h (1.3-9.3 h)
PAP adherence (per night)	Median 2.5 h/night (0.7-4.5)	0-3.8 h/night, mean 2.4-4.6 h/night	3.0 h (1.0-7.5 h/night)

See Table 1 legend for expansion of abbreviations.

patients who may have suspected OSA refuse to undergo additional testing for establishing an OSA diagnosis.<sup>44,69</sup> Guralnick et al<sup>69</sup> speculated that the inconvenience of an overnight in-laboratory PSG or even out-of-center sleep testing, the short time available between evaluation by the anesthesia team and the actual date of surgery, cost, underappreciation of the implications of undiagnosed and untreated OSA by patients and clinicians, lack of understanding of the consequences of untreated OSA, and unwillingness to use CPAP may have all contributed to the failure of surgical patients to accept and adhere to perioperative diagnosis and treatment of OSA. These reasons may explain why only approximately 45% of patients with newly diagnosed OSA were adherent to APAP therapy in the perioperative period.<sup>44,69</sup> Other factors that have been associated with reduced APAP adherence in the perioperative period include African American race, male gender, and depressive symptomatology.<sup>69</sup>

In two studies, the optimal level of APAP was  $9 \pm 2$  cm H<sub>2</sub>O in surgical patients with newly diagnosed OSA.<sup>44,69</sup> This information could be used empirically to prescribe the minimum and maximum pressure settings on APAP devices if clinicians need to prescribe APAP in the postoperative period for patients suspected of having OSA but who have not undergone formal sleep testing or PAP titration.

Postoperative CPAP utilization has been reported to be suboptimal even in patients with an established diagnosis of OSA. Gupta et al<sup>41</sup> found that only one-third of patients who were on home CPAP therapy used their CPAP during the postoperative stay in the hospital. Liao et al<sup>42</sup> found that only 63% of patients on home CPAP therapy received postoperative CPAP. Intensive education of health-care professionals and patients is needed to ensure that patients are instructed to bring their CPAP device to the hospital and to continue to use CPAP therapy during the vulnerable postoperative period. In lieu of patients bringing their own CPAP units, effective APAP therapy can be provided to the patient by using hospital APAP or CPAP devices.

### Who Are the Surgical Patients With OSA at Increased Risk?

It is not known which subgroups of patients with SDB are more likely to benefit from PAP therapy. Patients with obesity hypoventilation syndrome, overlap syndrome, patients with severe OSA (AHI > 30), and patients with a high arousal threshold with recurrent severe hypoxemia may possibly benefit from preoperative PAP therapy. Patients with OSA and unrecognized obesity hypoventilation syndrome or overlap syndrome (COPD and OSA) had higher risks of postoperative respiratory failure, heart failure, prolonged

intubation, and longer ICU and hospital length of stay than patients with nonhypercapnic OSA.<sup>71</sup> Therefore, hypercapnia can be an important risk modifier. Although many patients normally do not have measurements of arterial blood gases, high serum bicarbonate in venous blood can serve as a surrogate for hypercapnia and may help to identify patients with obesity hypoventilation syndrome.<sup>72-74</sup> Identifying this patient population is critical because CPAP use may not be sufficient and other advanced modes of PAP therapy such as bilevel PAP with or without a backup rate may have to be applied.

Recently, it was shown that 26% of patients without OSA (preoperative AHI < 5) developed moderate-to-severe SDB (AHI > 15) in the first 1 to 3 days after surgery.<sup>75</sup> In these patients, preoperative respiratory effort-related arousals may have converted to apneas or hypopneas in the postoperative period, likely because of increased upper airway collapsibility. The reasons behind increased upper airway collapsibility may be related to rostral fluid shifts and/or respiratory depression induced by opioids and sedatives.<sup>12,13,65,76,77</sup> In this study, preoperative respiratory disturbance index, rather than the AHI, and age were significant predictors of postoperative moderate-to-severe SDB.<sup>75</sup> As a result, it was suggested that in surgical patients, respiratory disturbance index may be more useful than AHI in diagnosing OSA.

Mutter et al<sup>30</sup> identified patients with more severe OSA (AHI > 30) to be at higher risk of adverse postoperative cardiopulmonary events, but it is not known whether AHI by itself is the best metric of OSA severity to risk stratify perioperative patients with OSA. Other metrics of OSA severity in the surgical patients such as mean preoperative overnight SpO<sub>2</sub>, oxygen desaturation index, and total sleep time below 90% SpO<sub>2</sub> may be useful as well. Chung et al<sup>60</sup> found that patients with mean preoperative overnight SpO<sub>2</sub> < 93%, oxygen desaturation index > 29 events/h or more than 7% total sleep time < 90% SpO<sub>2</sub> were at higher risk of postoperative adverse events.

Another less-recognized cause of sudden death in patients with OSA is arousal failure. It has been suggested that an obstructive sleep apneic event may not spontaneously terminate because of an ineffective arousal mechanism related to impaired chemosensitivity and/or opioid-induced respiratory depression, leading to profound cerebral hypoxemia and ultimately death.<sup>76,77</sup> Further research is necessary to determine the various

phenotypes of OSA and which metrics of SDB severity are likely to predict postoperative adverse events. Measures of hypoxemic exposure as well as hypercapnia need to be taken into account when risk-stratifying patients with SDB.<sup>60,78</sup>

## Should We Use CPAP to Treat Patients With Undiagnosed OSA?

Many anesthesiologists have become perioperative physicians; in this important role, they are instrumental in optimizing outcomes and minimizing complications in surgical patients. Preoperative clinic is a “teachable moment” for surgical patients with undiagnosed or untreated OSA. Patients with OSA have evidence of increased cardiopulmonary complications. There is preliminary evidence supporting that patients with OSA treated with CPAP have fewer postoperative cardiopulmonary complications.<sup>30,31</sup> Undiagnosed patients with severe OSA have two to threefold increased risk for cardiovascular and pulmonary complications.<sup>30</sup> Given the preponderance of data on long-term benefits and improved prognosis of patients with OSA with CPAP treatment, screening surgical patients for OSA and initiating PAP therapy in the perioperative period may be medically appropriate.<sup>79,80</sup>

With accumulating evidence from studies,<sup>3,12,13,21,22,24,25,30,31,81,82</sup> it may be ethically difficult to perform RCTs. Moreover, given the overall low rates of postoperative complications, another challenge is designing RCTs that are adequately powered to detect these clinically meaningful outcomes.<sup>18</sup> With the increased awareness of postoperative complications associated with OSA, researchers may face increasing rates of unwillingness on the part of patients and their physicians to participate in RCTs.<sup>56</sup> The field of perioperative medicine is not unused to these challenges; a similar dilemma regarding perioperative monitoring with pulse oximetry occurred in the 1980s. Because of the overall low rates of adverse events, RCTs have failed to show differences in postoperative complications, length of stay, or death between those monitored by oximetry and control subjects.<sup>83</sup> In spite of that, anesthesiologists have universally adopted monitoring patients with pulse oximetry in operating rooms and PACUs. Subsequently, patients have benefitted from increased safety with anesthesia despite the absence of positive findings of benefits from RCTs on oximetry monitoring. Another example is malignant hyperthermia (MH), a serious complication.<sup>84</sup> During the past few decades, surgical patients are screened for a



personal or family history of MH and an anesthesia protocol is followed.<sup>84</sup> Treatment with dantrolene is initiated after MH occurs.<sup>84</sup> These two historical perspectives (oximetry monitoring and MH recognition) may provide insights into how best to manage patients with OSA in the perioperative period, with the ultimate goal of increasing their safety. Surgical patients can be screened for sleep apnea, appropriate CPAP treatment may be given where appropriate, and postoperative monitoring can be provided.

### Who Might Have Benefits With CPAP?

Surgical patients with OSA adherent to CPAP therapy should continue their CPAP use postoperatively. The management of patients nonadherent to CPAP or suspected OSA is more challenging. It depends on preexisting comorbidities, types and urgency of surgery, requirement of postoperative opioids, and availability of postoperative monitoring. There is a high prevalence of OSA in surgical patients, which is in contrast with the very low incidence of critical postoperative respiratory events. The diagnosis of OSA per se cannot be considered a diagnostic marker for respiratory complications.<sup>85</sup> Certain pathophysiological features of OSA may enhance opioid induced ventilatory impairment resulting from respiratory compromise or suppression of the arousal response to airway obstruction. Respiratory depression may be more prominent in patients with OSA who have decreased ventilatory responses to hypoxia/hypercapnia stimuli and high arousal threshold with recurrent severe hypoxemia.<sup>85</sup> Patients should be informed that they have been identified as either having a high probability of OSA or as having a diagnosis of OSA with increased risk of postoperative complications. Patients, surgeons, and anesthesiologists should be jointly involved in the decision-making whether to have additional preoperative evaluations and/or consideration before surgery. In the bariatric surgical patients with a high prevalence of OSA, preparation for surgery with screening and CPAP treatment are routinely performed as part of the preoperative workup. Judgment and common sense should be used to manage patients with undiagnosed OSA or patients with OSA nonadherent to CPAP therapy. Individual evaluation is important to determine the best course of action. Referral to sleep medicine for CPAP therapy may have to be taken in the absence of overwhelming evidence from RCTs in certain groups of patients. Patients with severe OSA, COPD or overlap syndrome, obesity hypoventilation syndrome, or pulmonary hypertension would definitely benefit from

further evaluation and workup. Patients who have preoperative resting hypoxemia on room air with no known cardiopulmonary cause are potential candidates for further preoperative evaluation. Patients with decreased respiratory responses to hypoxia/hypercapnia stimuli and a high arousal threshold presenting with recurrent severe hypoxemia may benefit from preoperative CPAP.

### Research Questions

Despite important advances, many important and clinically relevant questions remain unanswered.<sup>47,78</sup> How should OSA be screened and diagnosed in surgical patients? Which phenotype of OSA would benefit from PAP therapy? When should we refer surgical patients who are nonadherent to CPAP or have suspected OSA? Should we refer these patients preoperatively and initiate CPAP therapy if needed? Should we refer these patients postoperatively and opt to minimize risk with perioperative precautions and postoperative monitoring? When is the optimal time to implement PAP therapy? How should we monitor OSA patients postoperatively? What are the best modalities of PAP therapy for perioperative use? What are the reasons for lack of adherence to PAP therapy and how can we improve adherence to PAP therapy? What are the obstacles to implementing a PAP protocol? What therapeutic options should be used in PAP-intolerant patients? What are the cost implication, cost-effectiveness, and cost-benefit considerations of preoperative diagnosis of OSA and implementation of PAP therapy? Without a doubt, more research is needed to provide answers to some of these clinically relevant questions. In the meantime, clinical acumen and a commonsense approach is needed to identify surgical patients with undiagnosed OSA who may be at risk for postoperative adverse events who could benefit from CPAP therapy and postoperative monitoring.

In conclusion, diagnosing OSA and using perioperative CPAP therapy may be effective interventions to reduce the incidence of postoperative adverse outcomes in patients with OSA undergoing surgery. Further research in this area is needed to determine whether this strategy has a positive effect on hospital resource utilization and reduction in cost of the health-care system.

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